

We claim:

1. A method of mapping a network of functional gene interactions relating to Alzheimer's disease, comprising the steps of:

5 (a) performing matings between (1) a first parent strain carrying a mutation in said Alzheimer's disease gene and (2) a series of parent strains each containing one of a series of genetic variations

to produce a series of test progeny, each of said  
10 test progeny carrying a mutation in said Alzheimer's disease gene and one of said series of genetic variations; and

15 (b) screening said series of test progeny for an altered phenotype relative to at least one sibling control, thereby localizing a gene that is a member of an Alzheimer's disease genetic network to one of said series of genetic variations.

2. The method of claim 1, further comprising  
20 identifying said gene that is a member of an Alzheimer's disease genetic network.

3. The method of claim 1, further comprising iteratively repeating steps (a) and (b), thereby identifying a network of functional gene interactions  
25 relating to Alzheimer's disease.

4. The method of claim 1, wherein the Alzheimer's disease gene is *amyloid precursor protein-like (Appl)*.

5. The method of claim 1, wherein the Alzheimer's disease gene is *presenilin* (*Psn*).

6. The method of claim 1, wherein the Alzheimer's disease gene is selected from the group consisting of  
5 *har38*, *dCrbA*, *dCrbB*,  $\alpha$ -*adaptin*, *garnet*, *shi*, *N*, *Su(H)1*,  
*Dl*, *mam* and *bib*.

7. The method of claim 1, wherein the series of genetic variations comprises at least twenty individual genetic variations.

10 8. The method of claim 1, wherein the series of genetic variations comprises at least one hundred individual genetic variations.

9. The method of claim 1, wherein the series  
15 of genetic variations comprises a genetic variation that maps to the X-chromosome.

10. The method of claim 1, wherein each of the genetic variations in the series maps to the X-chromosome.

20 11. The method of claim 1, wherein the series of genetic variations comprises a genetic variation that maps to an autosome.

12. The method of claim 1, wherein each of the genetic variations in the series maps to an autosome.

13. The method of claim 1, wherein each of the series of test progeny is doubly heterozygous for the mutation in the Alzheimer's disease gene and one of the series of genetic variations.

5

14. The method of claim 1, wherein at least one parental strain comprises a balancer chromosome.

15. The method of claim 1, wherein the parent strains are *Drosophilidae*.

10

16. The method of claim 15, wherein the parent strains are *Drosophila melanogaster*.

15

17. The method of claim 1, wherein the mutation in the Alzheimer's disease gene is selected from the group consisting of an amorph, hypomorph, antimorph, hypermorph and neomorph.

18. The method of claim 1, wherein the mutation in the Alzheimer's disease gene is a deficiency.

19. The method of claim 1, wherein the Alzheimer's disease gene maps to the X-chromosome.

20

20. The method of claim 1, wherein the Alzheimer's disease gene maps to an autosome.

21. The method of claim 1, wherein the phenotype is selected from the group consisting of viability, morphology and behavior.

22. A method of identifying a therapeutic agent for treating Alzheimer's disease, comprising the steps of:

(a) performing matings between a first parent 5 strain carrying a mutation in an Alzheimer's disease gene and a second parent strain containing a genetic variation, whereby test progeny are produced,

wherein, in the absence of an agent, the parent strains produce test progeny having an altered phenotype 10 relative to at least one sibling control;

(b) administering an agent to at least one strain selected from the group consisting of said first parent strain, said second parent strain and said test progeny; and

15 (c) assaying the test progeny for the altered phenotype,

wherein a modification of the altered phenotype producing a phenotype with more similarity to a wild type phenotype than the altered phenotype has to the wild type 20 phenotype indicates that the agent is a therapeutic agent.

23. The method of claim 22, wherein said modification is a complete or partial reversion of the altered phenotype.

25 24. The method of claim 22, wherein the Alzheimer's disease gene is *Appl*.

25. The method of claim 22, wherein the Alzheimer's disease gene is *Psn*.

26. The method of claim 22, wherein the Alzheimer's disease gene is selected from the group consisting of *har38*, *dCrbA*, *dCrbB*,  $\alpha$ -*adaptin*, *garnet*, *shi*, *N*, *Su(H)1*, *Dl*, *mam* and *bib*.

5 27. The method of claim 22, wherein the parent strains are *Drosophila melanogaster*.

28. The method of claim 22, wherein the altered phenotype is increased viability.

29. The method of claim 22, wherein said 10 altered phenotype is decreased viability.

30. An isolated nucleic acid molecule that is differentially expressed in *App1<sup>d</sup>* versus *App1<sup>+</sup>* *Drosophila melanogaster*, comprising a nucleic acid sequence having substantially the sequence of a nucleic acid sequence 15 selected from the group consisting of SEQ ID NOS: 1 to 63.

31. The isolated nucleic acid molecule of claim 30, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1 to 63.

20 ~~32a~~  
~~31.~~ An isolated nucleotide sequence, comprising at least 10 contiguous nucleotides of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1 to 63.

*Runde*  
*1/26*

*33*  
32. The isolated nucleotide sequence of claim 31, comprising at least 15 contiguous nucleotides of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1 to 63.

5 *34*  
33. An isolated nucleic acid molecule that is differentially expressed in *App1<sup>d</sup>* versus *App1<sup>+</sup>* *Drosophila melanogaster*, comprising a nucleic acid sequence having substantially the sequence of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 64

10 to 80.

*35*  
34. The isolated nucleic acid molecule of claim 33, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 64 to 80.

15 *36*  
35. An isolated nucleotide sequence, comprising at least 10 contiguous nucleotides of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 64 to 80.

20 *37*  
36. The isolated nucleotide sequence of claim 35, comprising at least 15 contiguous nucleotides of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 64 to 80.